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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,476	09/23/2003	Abraham Shahar	85189-498	4834

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EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,476	SHAHAR ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/23/03 and 4/14/0*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A response of 4/3/06 to a restriction requirement of 3/7/06 elected Group I claims 1-9, 21 and 32-35, and amended the claims of Group II to depend on the elected claims.

Due to the amendment, the claims of Group II will be examined with the claims of Group I.

Claims examined on merits are 1-35, which are all claims in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 and claims dependent thereon are confusing and unclear by claim 10 being unclear as to the meaning of "whereas the cells are cultured in or upon the matrix to form a combined gel". Cells cultured on the matrix involves a process, and it is unclear how this process further limits the matrix of claim 1. If process conditions are required to define the matrix, a complete process should be set forth containing clear, distinct and positive process steps. In line 2 of the claim, "cells other than cells of a neuronal explant" is

uncertain as to cells excluded. The meaning of "neuronal explant" is uncertain. In the last line of claim 10, the meaning of "to form a combined gel" is uncertain. Does this mean a combination of gels, or something else? Furthermore, how does the combined gel differ from the matrix of claim 1? There is no antecedent basis for the matrix of claim 1 being a gel, and no conditions have been required to change the matrix to a gel.

In claims 11-14, 16-18 and 20, reciting "types" or "type" after "cell" makes unclear the cells required. A cell that is a cell of type rather that a cell is relative and subjective. It would be uncertain as to characteristics a cell is a cell type and not a cell.

Claim 19 is unclear for reasons set forth above in regard to claim 10 by requiring cells cultured on the exposed surface of a combined hyaluronic acid laminin gel. What causes the matrix of claim 1 to be changed to a gel? Is a combined gel a combination of gels, or some other form of gel? Is the gel of claim 19 the matrix of claim 1, or a gel in addition to the matrix? Since claim 1 requires both hyaluronic acid and laminin, the purpose of again requiring hyaluronic acid and laminin in claim 19 is uncertain. Additionally, it is unclear how cells cultured on an exposed surface changes the matrix of claim 1.

Claims 21 and 22 are unclear how the implant differs from the matrix claim 1 or 10 since the implant fails to contain implant structure that will require the implant to be different from the matrix.

Claim 23 is unclear by requiring a method for preparing the matrix of claim 1, and not reciting steps that will produce the matrix. The steps of 23 do not require the bioactive compound or drug of claim 1, and they cannot be optional as in line 5 of claim 23 since they are required by claim 1. There is not antecedent basis in claim 1 for "structural components" in line 6 of claim 23, and the term "combined gel" is confusing for reasons set forth above. In line 2 of claim 23, there is not antecedent basis in claim 1 for "matrix according to claim 1 to be implanted in a human subject". It is uncertain how the process of claim 23 changes the matrix of claim 1 to be a matrix that is implanted.

Claim 25 is unclear how embedding cells in or on the gel occurs.

The recital of "combined gel" in claim 26 is confusing for reasons set forth above. Additionally, there is not antecedent basis in claim 1 for "exposed surface of the combined gel".

Claim 28 is unclear how it further limits claim 23 since the bioactive compound or drug required is already in claim 1. Since claim 23 depends on claim 1 and claim 28 depends on claim 23, again reciting in claim 28 the bioactive compound or drug does not further limit claim 23.

In line 2 of claim 32, there is not antecedent basis in claim 1 for an exposed surface of a gel.

In claim 33, there is not antecedent basis in claim 32 for "the exposed surfaces of the device".

Claims 34 and 35 are unclear how they further limit claims 32 and 33 by requiring the medical device of claim 32 or 33 to comprise a bioactive compound or drug since claim 33 depends on claim 32, which requires the matrix of claim 1 that requires the matrix to comprise a bioactive compound or drug. Since claim 1 already requires the bioactive compound or drug, how can again requiring the bioactive compound or drug in claims 34 and 35 be a further limitation?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-6, 8, 9, 21, 23, 24, 28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balazs et al (5,128,326) in view of Skubitz et al (5,703,205) and Zecchino et al (6,497,887 B1).

The claims are drawn to a biocompatible matrix comprising hyaluronic acid and laminin, and a bioactive compound or drug selected from a group including ascorbic acid and DHEA.

Balazs et al disclose a drug delivery system containing a cross-linked gel formed by cross-linking hyaluronic acid and a polymer together. The polymer can be a glycol protein (col 2, lines 19-23 and 45-49, and col 4, lines 26 and 58-62), and the gel can contain a drug to be delivered. The cross-linked gel can be used in combination with supports or substates (col 4, lines 54-57).

Skubitz et al disclose that laminin is a glycoprotein that occurs in basement membranes (col 1, lines 29-36). Laminin has various functions relating to cells (col 1, line 63 to col 2, line 24, and col 12, lines 4-38). A laminin polypeptide can promote wound healing (col 12, lines 4-7).

Zecchino et al disclose a membrane delivery system containing a biologically active agent for delivery. The agent can be ascorbic acid (col 5, line 41), or a hormone such as estrogen, progesterone or DHEA (col 5, lines 50-55). Other therapeutic agents can be also delivered (paragraph bridging cols 5 and 6).

It would have been obvious to use laminin as the glycoprotein of Balazs et al that is cross-linked with hyaluronic acid as suggested by

Skubitz et al disclosing that laminin is a glycoprotein and can have various functions including promoting wound healing that would have been expected to be advantageous when the delivery system of Balazs et al is used to delivery a drug to a wound. It would have been further obvious to use ascorbic acid or DHEA as the drug of Balazs et al to obtain their function as suggested by Zecchino et al disclosing a membrane delivery system for delivery of an active agent that can be ascorbic acid or DHEA. The viscosity of claim 4, and percentages of hyaluronic acid and laminin of claims 5 and 6 would have been matters of individual preference within the skill of the art. A structural component as in claim 9 would have been suggested by Balazs et al disclosing using the cross-linked gel in combination with a support or substrate (col 4, lines 54-47). The method for preparing the matrix of claim 23 would have been obvious from the method disclosed by Balazs et al for preparing a cross-linked gel containing a glycoprotein and hyaluronic acid.

Claim Rejections - 35 USC § 103

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 2, 4-6, 8, 9, 21, 23, 24, 28 and 30 above, and further in view of Brodsky et al (4,971,954).

The claim requires a sugar as an exogenous cross-linking agent.

Brodsky et al disclose cross-linking collagen by reacting amino groups of collagen with an aldehyde group of a reducing sugar (col 4, lines 19-60).

When using laminin as the glycoprotein of Balazs et al as set forth above, it would have been obvious to use a reducing sugar as the cross-linking agent of Balazs et al as suggested by Brodsky et al disclosing that the aldehyde group of a reducing sugar reacts with amino groups of collagen to cross-link the collagen since hyaluronic acid contains an amino group that would have been expected to react the reducing sugar in the same type of way as with collagen.

Claim Rejections - 35 USC § 103

Claims 7 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 2, 4-6, 8, 9, 21, 23, 24, 28 and 30 above, and further in view of Gao (6,927,204 B2).

The claims require bioactive compounds or drugs including IGF1.

Gao discloses a container containing a pharmaceutically acceptable carrier containing a cell proliferation-inducing amount of IGF1 (col 34, lines 34-40).

When using laminin as the glycoprotein of Balazs et al as set forth above, it would have been obvious to use IGF1 as the drug to be delivered to obtain the function of this drug to induce cell proliferation as disclosed by Gao.

Claim Rejections - 35 USC § 103

Claims 10-20, 22, 25-27 and 30-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 2, 4-6, 8, 9, 21, 23, 24, 28 and 30 above, and further in view of Valentini et al (5,939,323) and Shahar et al (WO 99/58042).

The claims require the matrix to contain cells resulting from cells being cultured in or upon the matrix.

Valentini et al disclose a scaffold formed of hyaluronic acid for use in tissue repair (paragraph bridging cols 1 and 2). The scaffold can contain bioactive agents (col 3, lines 7-19, and col 6, lines 19-49) such as a growth factor (col 6, lines 36-37). Cells can be seeded on the scaffold and grown on the scaffold (col 3, lines 53-62, col 4, lines 3-10, and paragraph bridging cols 7 and 8). Various types of cells can be used depending on the type of tissue repaired, and the cells can be stem cells (col 7, line 42). The scaffold can be a two-phase scaffold by combining a biodegradable polymer such as polylactic acid or polyglycolic acid with the hyaluronic acid (col 3, lines 41-51).

Shahar et al disclose culturing neuronal cells in a matrix gel formed of hyaluronic acid and laminin to form a neuronal implant (paragraph bridging pages 16 and 17, and page 17, line 7, to page 18, line 3).

When using laminin as the glycoprotein of Balazs et al as set forth above, it would have been obvious to culture cells on the gel to provide cells on the gel for implanting as suggested by Valentini et al forming an implant by culturing cells on a hyaluronic acid scaffold and by Shahar et al producing an implant by culturing cells on gel formed of hyaluronic acid and laminin. While Shahar et al culture only neuronal cells, it would have been apparent from Valentini et al

that other cells can be cultured on the gel depending on the type of tissue repaired.

Claim Rejections - 35 USC § 103

Claims 1, 2, 4-6, 9-28 and 31-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valentini et al in view of Balazs et al and Skubitz et al, and if necessary in further view of Shahar et al.

The invention and references are described above.

It would have been obvious a cross-link a glycoprotein and hyaluronic acid together to form the scaffold of Valentini et al as suggested by Balazs et al cross-linking hyaluronic acid and a glycoprotein together, and it would have been obvious to use laminin as the glycoprotein as suggested by Skubitz et al disclosing that laminin is a glycoprotein, and has various functions including enhancing wound healing. The viscosity of claim 4, and percentages of hyaluronic acid and laminin in claims 5 and 6 would have been matters of individual preference within the skill of the art. A structural component as in claim 9 would have been suggested by Balazs et al disclosing using the cross-linked gel in combination with a support or substrate (col 4, lines 54-47). The method for preparing the matrix of claim 23 would have been obvious from the method disclosed by Balazs et al for preparing a cross-linked gel containing a glycoprotein and hyaluronic acid. If needed, Shahar et al would have further suggested growing cells on a scaffold formed of hyaluronic acid and laminin.

Claim Rejections - 35 USC § 103

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 2, 4-6, 9-28 and 31-35 above, and further in view of Brodsky et al.

The invention and references are described above.

When cross-linking laminin and hyaluronic acid together to form the scaffold of Valentini et al as set forth above, it would have been obvious to use a reducing sugar as a cross-linking agent as suggested by Brodsky et al disclosing that the aldehyde group of a reducing sugar reacts with amino groups of collagen to cross-link the collagen since hyaluronic acid contains an amino group that would have been expected to react with the reducing sugar in the same type of way as with collagen.

Claim Rejections - 35 USC § 103

Claims 7 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 2, 4-6, 9-28 and 31-35 above, and further in view of Gao.

The invention and references are described above.

When cross-linking laminin and hyaluronic acid together to form the scaffold of Valentini et al containing a bioactive agent as set forth above, it would have been obvious to use IGF1 as the bioactive agent to obtain the function of this agent to induce cell proliferation as disclosed by Gao.

Claim Rejections - 35 USC § 103

Claims 8 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1, 2, 4-6, 9-28 and 31-35 above, and further in view of Zecchino et al.

The invention and references are described above.

When cross-linking laminin and hyaluronic acid together to form the scaffold of Valentini et al containing a bioactive agent as set forth above, it would have been obvious to use ascorbic acid or DHEA as the bioactive agent to obtain their function as suggested by Zecchino et al disclosing a membrane delivery system for delivery of an active agent that can be ascorbic acid or DHEA.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
6/13/06